https://doi.org/10.47262/BL/9.1.20230220

Review article
2026 | Volume 12 | Issue [illegible] | Pages 1-13

ARTICLEINFO

Received
October 28, 2025
Revised
December 02, 2025
Accepted
January 06, 2026

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Keywords
COVID-19 pandemic
Healthcare workers
Educational system
SARS-CoV-2
Psychological challenges

How to Cite
Khan MF, Waheed K, Mehtab M, Raza MA. The COVID-19 pandemic: A comprehensive biomedical review of its impact on healthcare, employment, and academic sectors. Biomedical Letters 2026; 12(1): 1-13.

The COVID-19 pandemic: A comprehensive biomedical review of its impact on healthcare, employment, and academic sectors

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Abstract

The coronavirus outbreak emerged as a severe pandemic and caused a global emergency. It resulted in the death of more than one million people worldwide. Coronavirus was first reported in 2019 at the seafood market in Wuhan, China. Coronavirus belongs to the family *Coronaviridae* and the subfamily of *Coronavirinae*. It is a single-stranded RNA, non-segmented, and enveloped virus. Its genome is the largest among the RNA viruses. The RT-PCR technique is used for the diagnosis of COVID-19, while bronchoscopy was also used initially; however, patient and medical staff were at high risk because both are vulnerable to the disease. Initially, there was no specific treatment for COVID-19, and the patients were managed based on their symptoms. Maintaining proper physical distance and using face masks were the initial prevention measures adopted to control the spread of the coronavirus. COVID-19 also had severe effects on the health sector. It has not only affected patients but also significantly impacted healthcare workers and staff. Patients became vulnerable to conditions such as insomnia, depression, and anxiety. Healthcare workers faced physical, emotional, and psychological challenges. The workload on healthcare workers increased due to the rising number of patients, which reduced work efficiency and increased stress and anxiety levels. The suicide rate also increased from 1% to 145% worldwide. Initially, hospitals were not prepared for such a pandemic outbreak and faced multiple challenges,

including shortage of testing kits, ventilators, hospital beds, and intensive care units. The COVID-19 outbreak also affected the education system, with over 1.7 billion students being disturbed. Schools were completely shut down, and higher education institutions such as colleges and universities shifted to a hybrid model, including online education. Overall, lifestyles were profoundly altered after the pandemic outbreak, as it affected healthcare, education, and the global economy.

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Introduction

A mystifying pneumonia characterized by dry cough, high fever, and some gastrointestinal symptoms emerged in the seafood market in Wuhan in December 2019 [1]. The epidemic was initially reported in December 2019, affecting approximately 66% of the market staff. The market was placed under liquidation on January 1, 2020, as the local healthcare authorities declared an epidemiological alert on December 31, 2019. Despite these measures, thousands of people across different provinces of China, including Hubie, Zhejiang, Guangdong, Henan, and Hunan, as well as major cities such as Beijing and Shanghai, were affected by the uncontrolled spread of the disease [2]. Moreover, the disease rapidly spread to other countries, including Thailand, Japan, the Republic of Korea, Vietnam, Germany, the United States, and Singapore. According to data documented by the World Health Organization (WHO) as of February 6, 2020, a total of 28,276 confirmed cases and 565 deaths were reported globally. The infectious agent responsible for the epidemic was later identified as a novel beta-coronavirus, named 2019 novel coronavirus (2019-nCoV) [3].

Coronaviruses are classified under the taxonomic family *Coronaviridae*. These viruses contain a positive single-stranded RNA genome enclosed within an envelope [4]. Coronaviruses are further categorized into four different genera: Alpha, Beta, Gamma, and Delta coronavirus. To date, at least seven different types of human coronaviruses (HCoVs) have been identified, most of coronavirus genera [5]. The Alpha coronaviruses include HCoV-NL63 and HCoV-229E, whereas the Beta coronaviruses include HCoV-OC43, HCoV-HKU1, SARS-CoV (severe acute respiratory syndrome coronavirus), MERS-CoV (Middle East respiratory syndrome-related coronavirus), and the most notable and well-recognized SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) [6, 7].

The SARS coronavirus, which fulfilled Koch's postulates, first originated in Guangdong province in southeast China in 2003, with a mortality rate ranging from 10% to 15% [5]. Although substantial advancements have been made in medical science and healthcare infrastructure since then, no specific treatment or vaccine has been available for SARS [8]. Another coronavirus outbreak emerged in the Middle East in 2012, exhibiting clinical characteristics similar to the 2003 outbreak [9]. Although both outbreaks were caused by coronaviruses, MERS was believed involve dromedary camels as an intermediate host and exhibited a significant higher fatality rate of 37%. SARS and MERS typically begin with non-specific clinical manifestations, primary fever and respiratory symptoms. Hospital staff lacking adequate protective measures and exposed to patient's respiratory droplets or bodily fluids are particularly vulnerable to nosocomial transmission. In addition, SARS, MERS, and COVID-19 cases associated with international travel have been widely documented [10, 11].

Structure of SARS-CoV-2

The coronavirus, or SARS-COV-2, belongs to the family *Coronaviridae* and the subfamily of *Coronavirinae* [12, 13]. SARS-CoV-2 is a single-stranded RNA (ssRNA) virus; it is non-segmented and enveloped, with an average length ranging from 26 kb to 36 kb. At this size, the coronavirus genome is the largest among RNA viruses. Under an electron microscope (EM), the virus appears spherical in shape. Long spike projections, measuring approximately 9-12 nm in length, are embedded on the viral surface, giving the virion a solar-like appearance [5]. The diameter of the virus ranges from 60 to 140 nm. Several structural similarities have been observed between SARS-CoV-2 and other members of the *Coronaviridae* family [14].

The coronavirus genome is associated with the nucleocapsid protein (N) and encodes three major capsid-associated proteins: enveloped protein (E), spike protein (S), and membrane protein (M) [15]. According to current observations, the estimated size of SARS-CoV-2 is about 29.9 kb [14]. SARS-CoV-2 encodes a total of twenty (20) proteins, which are broadly classified into structural and non-structural proteins. Among these, four are structural proteins (S, M, N, and E), while the remaining sixteen are classified as non-structural proteins (nsp1-nsp16).

Nsp1 acts as a bridge between viral replication and RNA processing. Nsp2 is involved in modulating the host cell survival signaling pathway. The translated viral polyproteins are cleaved into functional units by NSPs. Nsp4 contributes to endoplasmic reticulum (ER) membrane and contains transmembrane domain 2 (TM2). Nsp5 facilities the processing of polyprotein during viral replication. Nsp6 is a putative transmembrane protein. Nsp7 and Nsp8 are involved in template-primer RNA binding and interact with Nsp12. Nsp9 functions as an ssRNA-binding protein. Nsp10 plays a critical role in viral mRNA cap methylation. The RNA-dependent RNA-polymerase (RdRp), essential for viral replication and transcription, is enclosed by Nsp12. Nsp13 contains ATPase and zinc-binding domains and participates in the transcription and replication processes.

Nsp14 possesses proofreading exoribonuclease activity, while Nsp15 exhibits Mn^{2+}-dependent endoribonuclease activity, Nsp16 functions as a 2’-O-ribose methyltransferase [16, 17].

Recent studies have demonstrated that certain NSPs exert regulatory effects on host translation, mRNA splicing, and protein trafficking, thereby suppressing host defense mechanisms. Upon SARS-CoV-2 infection, Nsp16 suppresses host mRNA splicing by binding mRNA recognition domains of the U1 and U2 small nuclear RNAs (snRNAs) [18]. Nsp1 interferes with host mRNA translation by binding to the 18S ribosomal RNA at the mRNA entry channel of the ribosome. Additionally, Nsp8 and Nsp9 interact with 7SL RNA within the signal recognition particle, disrupting protein trafficking to the cell membrane [19, 20].

Diagnosis

Among the different diagnoses of viral pneumonia commonly accompanied by a flu-like illness, symptoms similar to COVID-19 may also arise from other respiratory viral pathogens such as influenza, parainfluenza, adenovirus, respiratory syncytial virus (RSV), and metapneumovirus. Other possible causative agents include *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. Therefore, it is necessary to carefully scrutinize travel history and possible contact with natural environmental vectors during the assessment of individuals who have been in an epidemic area. In addition, the use of commercial diagnostic tools for respiratory syndromes, such as FilmArray Respiratory Panel, sputum tests, and

bronchoscopy, which can identify multiple causative pathogens, may help accelerate clinical decision-making and improve diagnostic accuracy [1, 21].

Nasal swabs, bronchoalveolar lavage (BAL), or tracheal aspirate specimens are used for diagnosis through the RT-PCR technique. The predominant and most commonly used diagnosis method involves collecting samples from the upper respiratory tract through oropharyngeal and nasopharyngeal swabs. The use of bronchoscopy places both patients and medical staff at high risk of infection due to aerosol generation; therefore, this method is generally not recommended [22]. Bronchoscopy may be considered only for intubated patients under specific circumstances, such as when upper respiratory tract samples are negative or when results from other diagnostic methods would alter clinical management. Nevertheless, in case of uncertain diagnosis and when safety criteria are met, bronchoscopy may still be employed. As an alternative to bronchoscopy, healthcare providers may use non-BAL and tracheal aspiration to collect respiratory samples from intubated patients [23].

Despite the limited availability of RNA data, SARS-CoV-2 RNA has been detected in samples obtained from both the upper and lower respiratory tracts. The virus has also been successfully isolated in cell cultures containing secretions from the upper respiratory tract and BAL samples [24]. Zou and colleagues reported that samples collected from the upper respiratory tract exhibited higher levels of SARS-CoV-2 RNA, with lower cycle threshold values, during the first three days after symptom onset compared to nasal samples. Additionally, samples from the upper respiratory tract of asymptomatic individuals also showed notable levels of SARS-CoV-2 RNA [25]. Several investigations have reported that SARS-CoV-2 RNA can also be detected in stool and blood samples [24]. The duration for which SARS-CoV-2 RNA persists in tissues outside the lungs, including both the upper and lower respiratory tracts, remains uncertain. It is possible that viral RNA may remain detectable for several weeks after infection, similar to observations in SARS-CoV and MERS-CoV cases. Viable SARS-CoV has been isolated from stool, urine, respiratory tract, and blood samples [1, 24, 26, 27].

The RT-PCR test demonstrates very high specificity; however, contamination of swab samples may lead to false-positive results, particularly in patients with respiratory conditions [28]. The estimated sensitivity ranges from 66 to 80%, although it remains uncertain. In individuals with high exposure risk, a single negative RT-PCR test for SARS-CoV-2 may not be sufficient to rule out infection. In such cases, more invasive diagnostic approaches, such as BAL, may be considered [29].

Treatment

In 2019, when the first case of coronavirus was reported, there was no specific medicine or definitive treatment available for the disease. Initially, COVID-19 was managed symptomatically and through palliative care, such as monitoring vital signs, managing loss of taste, maintaining blood pressure and oxygen saturation levels, and treating complications, including organ failure and secondary infections. During the early stages of the pandemic, the mortality rate was high; therefore, extensive investigations and therapeutic trials were initiated.

Remdesivir is a drug developed by *Gilead Sciences, Inc*. It is a novel nucleotide analogue prodrug that was initially developed for the treatment of hepatitis C and was later evaluated for Ebola and SARS. At the time, it was an unapproved antiviral drug. When the first case of

2019-nCoV was reported in the United States in 2019, remdesivir was administered to the patient. By the 11th day of treatment, a reduction in disease severity was observed, resulting in clinical improvement. Subsequently, this drug entered clinical trials to determine its safety and efficacy for the treatment of patients infected with 2019-nCoV [30].

Convalescent Therapy involves the use of plasma obtained from the blood of recovered patients, a strategy similar to passive immunization. Previous studies on MERS demonstrated that interferon-beta/ribavirin combination therapy, convalescent plasma, and lopinavir may offer potential benefit. However, outcomes in COVID-19 cases may differ due to the lack of prior experience and the absence of randomized controlled clinical trials during the early phases of the pandemic [31]. SARS was previously treated using ribavirin and lopinavir/ritonavir, which showed positive results [32]. According to various studies, lopinavir and ribavirin demonstrated *in vitro* antiviral efficacy. The reported effective concentrations (4 and 50 µg/mL, respectively) showed antiviral activity within 48 hours. Additionally, structural similarities were identified between the insertion sites of the 2019-nCoV spike protein, Gag, and HIV-1, suggesting potential therapeutic relevance [33]. During the initial stages of the pandemic, no specific vaccines were available for COVID-19. As the pandemic progressed, extensive research and investigations were conducted. Initially, the spike protein was considered a potential vaccine target; however, further evaluation was required for human use. Subsequently, several vaccines were developed by the pharmaceutical companies, including Pfizer/BioNTech, Sinopharm, Sinovac, Moderna, CanSino, and Oxford/AstraZeneca.

Prevention

As there was no established treatment for COVID-19 initially, efforts were focused on reducing further transmission and preventing infection. Standard operating procedures (SOPs) for the general public included minimizing travel or completely avoiding travel to areas experiencing COVID-19 outbreaks. Individuals with a recent travel history within the previous two weeks from a pandemic-affected area were required to follow specific SOPs. These individuals were advised to undergo a 14-day isolation period, during which continuous monitoring of body temperature and self-surveillance were performed. If COVID-19 symptoms were observed in an individual, the patient was transferred to an isolation center for 14 days, and the isolation room was required to be well-ventilated. After completing the 14-day isolation period, if no symptoms were observed and the two consecutive negative tests confirmed the absence of COVID-19 infection, the individual could be released from isolation. For healthcare workers, strict protocols were implemented. They were required to wear appropriate protective equipment and be properly trained in its use. Special cases were needed while removing protective gear, particularly when working around confirmed patients [34].

Additionally, protective measures were required during high-risk procedures such as endotracheal intubation, endoscopy, and Ambu bagging. If a healthcare worker came into contact with blood or body fluid from an unprotected patient, the exposed area was required to be washed thoroughly with water and soap, followed by health monitoring for the subsequent 14 days. For deceased patients, preventive measures included burial or cremation to limit further transmission.

Heat and steam were reported to show effectiveness in inactivating COVID-19. Several active ingredients were identified as effective against the virus, including

ethyl alcohol (70%), chloroxylenol (0.24%), isopropanol (50%), sodium hypochlorite (0.1%-0.5%), benzalkonium chloride (0.05%), povidone-iodine (1% iodine), cresol soap (1%), and hydrogen peroxide (0.5%-7.0%). These agents were effective due to the virus's vulnerability to their active ingredients. Household bleach (5.25%) was recommended for cleaning blood spills or bodily fluid contaminated with the virus, consistent with WHO guidelines previously issued for Ebola virus disinfection.

COVID-19 is a zoonotic disease with a mortality rate that varies from low to high. In the absence of effective treatment during the early stages of the pandemic, avoiding contact with infected individuals remained the primary preventive strategy. Supportive care was the only available option to manage the disease. Although numerous trials and experiments were conducted to control the outbreak, strict monitoring of individuals with travel history and minimizing contact with infected patients were the most effective preventive measures. Finally, healthcare workers needed to remain aware of the risks associated with the infection and follow appropriate protective measures when managing infected patients.

COVID-19's effects on the health sector

The emergence of the novel coronavirus led to a global pandemic that disrupted societies and economies worldwide. COVID-19 significantly affected people's health, leading to increased levels of anxiety, depression, and insomnia [35]. Social routines were severely disturbed due to lockdown measures, which restricted travel and confined individuals to a single location. As a result, many people experienced frustration and psychological stress. The lack of physical activities during the COVID-19 pandemic also contributed to weight gain, as individuals remained indoors and engaged in sedentary lifestyles [36]. Individuals presenting with fever and lower respiratory tract symptoms, particularly those residing in or having a travel history to countries such as China, South Korea, Italy, Iran, and Japan, were considered primary suspected cases of COVID-19 infection [37]. Owing to the rapid spread and severity of the disease, the WHO declared COVID-19 a global health emergency [38].

Physical and psychological effects of COVID-19

Healthcare workers faced not only physical but also emotional and psychological challenges during the COVID-19 pandemic. COVID-19 significantly affected the daily activities and productivity of medical staff and doctors due to multiple contributing factors, including increased workload and fear of infection [36]. More than one-third of individuals reported experiencing some level of anxiety, while insomnia symptoms were reported in 33.9% of the population. Levels of anxiety and depression varied significantly across different professions, with nurses experiencing a higher prevalence of symptoms related to abnormal stress, depression, and severe clinical insomnia [39]. In one study, 53 out of 230 healthcare workers who completed the mental health assessment scales were found to have psychological and mental health problems.

The findings also indicate that female healthcare workers were more likely to experience mental health issues than their male counterparts. Another study reported that psychological conditions affecting healthcare workers included general anxiety (23–44%), mild anxiety (16.09%), severe anxiety (2.17%), moderate anxiety (4.78%), depression (50.4%), stress disorder (27.4–71%), and insomnia (34.0%) [40].

Work overload

Due to the increased workload and extended working hours, the productivity of healthcare workers decreased significantly [41]. Work is an important aspect of life; when performed in appropriate amounts, it benefits both physical and mental health. However, excessive workload can lead to stress, anxiety, and depression, resulting in emotional problems and a substantial decline in employees' self-efficacy and work performance [42]. Healthcare workers were compelled to adopt new practices and procedures to manage COVID-19 cases. Their motivation declined, and their mental health became unstable due to the fear, uncertainty, and risks associated with COVID-19 infection [43].

Anxiety and depression

Mental illnesses such as anxiety and depression have a significant impact on both individuals and society. The COVID-19 pandemic has had a detrimental effect on mental health, leading to increased feelings of anxiety and depression among the general population [44]. Depression is characterized by feelings of helplessness, low energy, reduced motivation, hopelessness, and suicidal thoughts, whereas anxiety is associated with mood disturbances, weight loss, loss of appetite, and persistent thoughts of death [45].

The onset of the pandemic caused widespread stress, resulting in elevated levels of anxiety and depression. Several factors contributed to this situation. People were isolated from their communities and confined to their homes, leaving them with limited activities and social engagement, which increased psychological vulnerability. Although social distancing was essential to prevent disease transmission, it also intensified feelings of loneliness and isolation [46]. Additionally, the pandemic caused severe economic challenges, including job losses and uncertainty about the future. Financial instability due to lockdowns, loss of income, and job insecurity further exacerbated mental health issues. Fear of becoming infected also contributed to heightened anxiety and psychological distress [47]. Collectively, these factors made individuals feel helpless and out of control, increasing their susceptibility to anxiety and depression. Among the healthcare personnel, increased workload, fear of infection, and prolonged lockdowns resulted in a high prevalence of anxiety, depression, and occupational burnout [48].

Social isolation and loneliness

Social isolation and loneliness refer to the feeling of being alone and lacking meaningful social interaction, which is often distressing. Measures such as social distancing and lockdowns significantly limited interpersonal connections, leading to increased feelings of loneliness during the COVID-19 pandemic [49]. Social isolation and loneliness are strongly associated with anxiety, depression, and suicidal thoughts. Numerous studies have shown that individuals experiencing higher levels of loneliness are more likely to report elevated levels of anxiety and depression.

Excessive levels of these feelings can promote suicidal thoughts [50]. Loneliness is the subjective experience of being alone, whereas social isolation is the objective condition resulting from limited social contacts. Even before the COVID-19 pandemic, social isolation and loneliness were highly prevalent across China, the United States, England, and other European countries, to the extent that they were described as a behavioral epidemic [51].

Studies indicate that loneliness is directly associated with negative physiological effects, including elevated systolic blood pressure and an increased risk of heart disease. Even among middle-aged individuals without a prior history of

myocardial infarction, social isolation and loneliness have been linked to higher mortality related to coronary artery disease. Furthermore, social isolation is associated with a high risk of dementia, an increased incidence of coronary heart disease, and a higher risk of stroke, with these risks being 50%, 29%, and 32% higher, respectively [52]. To reduce viral transmission, social contacts were restricted during the pandemic. Alternative communication methods, such as video calls and phone conversations, replaced face-to-face interactions; however, these methods often resulted in a reduced sense of closeness and intimacy and an increased feeling of loneliness among individuals [52, 53]. It is reasonable to assume that social isolation and loneliness increased during the pandemic, negatively affecting the overall quality of life [52]. Children and adolescents were particularly affected by social exclusion and became vulnerable to acute anxiety and sadness [54].

Insomnia

Mental health was severely affected during the COVID-19 pandemic, particularly sleep patterns and the prevalence of insomnia [55]. Sleep is essential for maintaining health, and insufficient sleep can have serious adverse effects [56]. Several factors disrupted sleep habits during the pandemic, including changes in daily routines, elevated stress levels, disturbed work schedules, prolonged time spent at home, increased screen exposure from computers and streaming platforms, and reduced social interaction. Collectively, these factors contributed to the development of insomnia. Excessive exposure to screen light has been shown to interfere with sleep cycles and contribute to sleep disorders, including insomnia [57]. Insomnia symptoms are not limited by gender or age and can affect individuals of all demographics. According to a 2020 report, the prevalence of insomnia increased from 15.7% to 23.6% during the pandemic [58]. Various reports and surveys indicate that COVID-19 disrupts sleep patterns and increases insomnia prevalence by more than 36% worldwide, 35% in Pakistan, over 24% in England, more than 33% in the United States, and 19% in France and China [55]. During the pandemic, 37% of healthcare workers in Taiwan reported experiencing insomnia, compared to only 4.7% in the general population [59].

Burnout

Burnout refers to a state of exhaustion resulting from prolonged exposure to excessive emotional, physical, and mental stress [60]. Although stress contributes to burnout, the two conditions are distinct. Stress arises from excessive demands on time, energy, and mental or physical capacity, whereas burnout develops when such stress is chronic and unmanaged [61]. Factors contributing to burnout include unmanageable workload, lack of communication, insufficient support, overwhelming responsibilities, and immense deadline pressures.

In China, 220 healthcare workers were diagnosed with burnout during the COVID-19 pandemic. Interestingly, frontline healthcare workers exhibited lower levels of burnout and expressed less concern about infection compared to healthcare workers assigned to regular wards. Two explanations were proposed: first, frontline workers felt they had greater control over the situation and were more directly involved in the decision-making process [62]. Another possible explanation is that frontline staff received timely information, allowing for better situational awareness. In contrast, healthcare workers on regular wards lacked clear information and realistic expectations, which heightened fear and uncertainty, increasing their susceptibility to burnout [62-64].

Health management

The widespread transmission of the coronavirus has profoundly affected healthcare systems worldwide. It has caused an unpredictable global crisis and prompted innovative responses to ensure continuity of care [65]. As the pandemic expanded, healthcare management had to reorganize services to maintain care delivery while simultaneously implementing measures to protect both patients and medical staff. Major challenges faced by healthcare personnel and administrators included a shortage of ventilators, testing kits, hospital beds, personal protective equipment, intensive care units, and essential medication [66].

Healthcare professionals working in emergency departments, critical care units, public health, primary care, and emergency services were susceptible to infection [67]. This heightened risk to healthcare workers was officially recognized by the WHO. In Pakistan, the primary challenges faced by healthcare management and workers included inadequate infrastructure, insufficient protective equipment, and a lack of proper training [68]. Testing and diagnosis were delayed due to the rapid spread of the disease. Additionally, staff shortage combined with a growing number of patients led to increased illness among healthcare workers, placing them under immense pressure [69].

Telemedicine emerged as an essential tool for delivering healthcare services while minimizing the risk of viral transmission. Due to the shortage of medical officers and restrictions imposed by lockdowns, virtual visits, digital health platforms, and remote consultations facilitated access to healthcare, especially in rural areas [70]. Prevention and control measures emphasized the use of personal protective equipment, strict sanitation protocols, and physical distancing, which became critical components of healthcare delivery to control the transmission [71]. Furthermore, 41.2% of hospitals identified the inability of public health organizations to receive data electronically as a major obstacle. Interface-related challenges, including system complexity and cost, were reported by 31.9% of hospitals as the next most common issue. Additional barriers included inconsistent terminology standards across hospitals, inefficiencies in electronic data transmission (8.3%), and the inability to extract data from electronic health records (14.7%) [72].

Suicide

Suicide is defined as the act of ending one's life to escape pain and suffering. During the COVID-19 period, suicide emerged as a significant public health concern due to emotional disturbance, anxiety, and depression. In addition, social isolation, loneliness, and loss of employment were major contributing factors leading to suicidal behavior [73]. According to a survey, having no friends and living alone for extended periods significantly increased suicidal thoughts and attempts [74]. During the pandemic, suicide rates reportedly increased from 1% to 145% worldwide. Most suicide attempts (79%) occurred in low and middle-income countries [75].

COVID-19's Impact on the Education System

The coronavirus pandemic, declared a global health emergency, has profoundly impacted education systems worldwide. On March 27, 2020, COVID-19-related school closures disrupted the education of 1.725 billion students globally [76]. National and state governments initiated widespread closure of schools and colleges to curb the spread and transmission of the virus. During the second week of March 2020, public announcements were made to avoid gatherings as a preventive measure against infection spread [77].

Initially, schools were closed for one month by the state governments; however, the closure period was repeatedly extended due to the rapid spread of COVID-19, leading to uncertainty about reopening timelines [78]. As a result, several critical activities, including competitive examinations, board examinations, and university entrance tests, were postponed or delayed [79]. At that time, institutional closure and lockdowns were considered the only effective measures to limit the outbreak. The worldwide closure of education institutes affected not only students' learning outcomes but also economic growth. COVID-19 significantly altered traditional education systems, forcing a shift towards alternative learning methods [77]. According to the United Nations Educational, Scientific, and Cultural Organization (UNESCO), 87% of students worldwide are affected by school closures, impacting over 1.5 billion students across 195 countries. In addition, the pandemic caused poor market cash flow, losses in domestic and international trade, and restrictions on travel. It also disrupted cultural events, increased stress levels, and led to the closure of hotels, lodging facilities, places of worship, and educational institutions [77].

Impacts of COVID-19 on the School System

Schools are structured environments for teaching and learning, where children not only acquire knowledge but also develop social awareness and essential social skills. Schools play a vital role in fostering these skills and supporting children's overall development. The primary purpose of attending school is to enhance a child's abilities and competencies. While regular school attendance benefits children, the absence of schooling can have adverse effects on them [77]. School closure significantly affected children's skill development and disrupted traditional teaching methodologies. These schools created challenges for students, parents, and teachers alike. In Pakistan, only a limited number of private schools were able to support online learning by adopting digital teaching techniques [80]. In such schools, children continued their education through online classes. Conversely, many low-income private and public schools remained closed. Students' learning is being interfered with by it. The shift in teaching methods also placed additional pressure on parents who had to manage multiple responsibilities. To curb the spread of infection, most countries temporarily closed nurseries, daycare centers, elementary and secondary schools, colleges, and universities [80, 81].

COVID-19's effects on higher education

The closing of universities and other higher education institutions also had an impact on students' education. Online learning methodologies are used to maintain continuity in education, and universities use online learning Management Software and e-learning platforms [82]. Higher education plays a critical role in economic growth; however, this sector was significantly compromised during the COVID-19 pandemic. The worldwide closure of institutions has reduced the demand for international higher education [77]. Due to COVID-19, graduates are facing problems in getting jobs, and at this time, unemployment is at a higher rate. In institutes and universities, the teaching methods have changed due to the lockdown. The education system was transformed from the old chalk method to new technology. Online systems are trying to overcome the education loss from lockdown [77, 82]. The current study summarizes the biological impact of SARS-CoV-2 infection, healthcare system overload, psychological consequences, and disruptions in educational systems

and global socioeconomic stability (**Fig. 1**).

Impacts of COVID-19 on students, parents, and teachers

The pandemic has not only affected students but also their parents and teachers. COVID-19 has enhanced social inequality in educational institutions [82]. Students from rich families were attending schools with high digital infrastructure, while students from poor and middle-class families were deprived of these facilities. Students during COVID-19 have faced mental challenges and social separation. Parents have faced challenges regarding balancing their work and family care, while teachers had to adopt new teaching methods and introduce new technologies, leading to overall mental disturbance [83]. COVID-19 showed significant impacts across major sectors (**Table 1**).

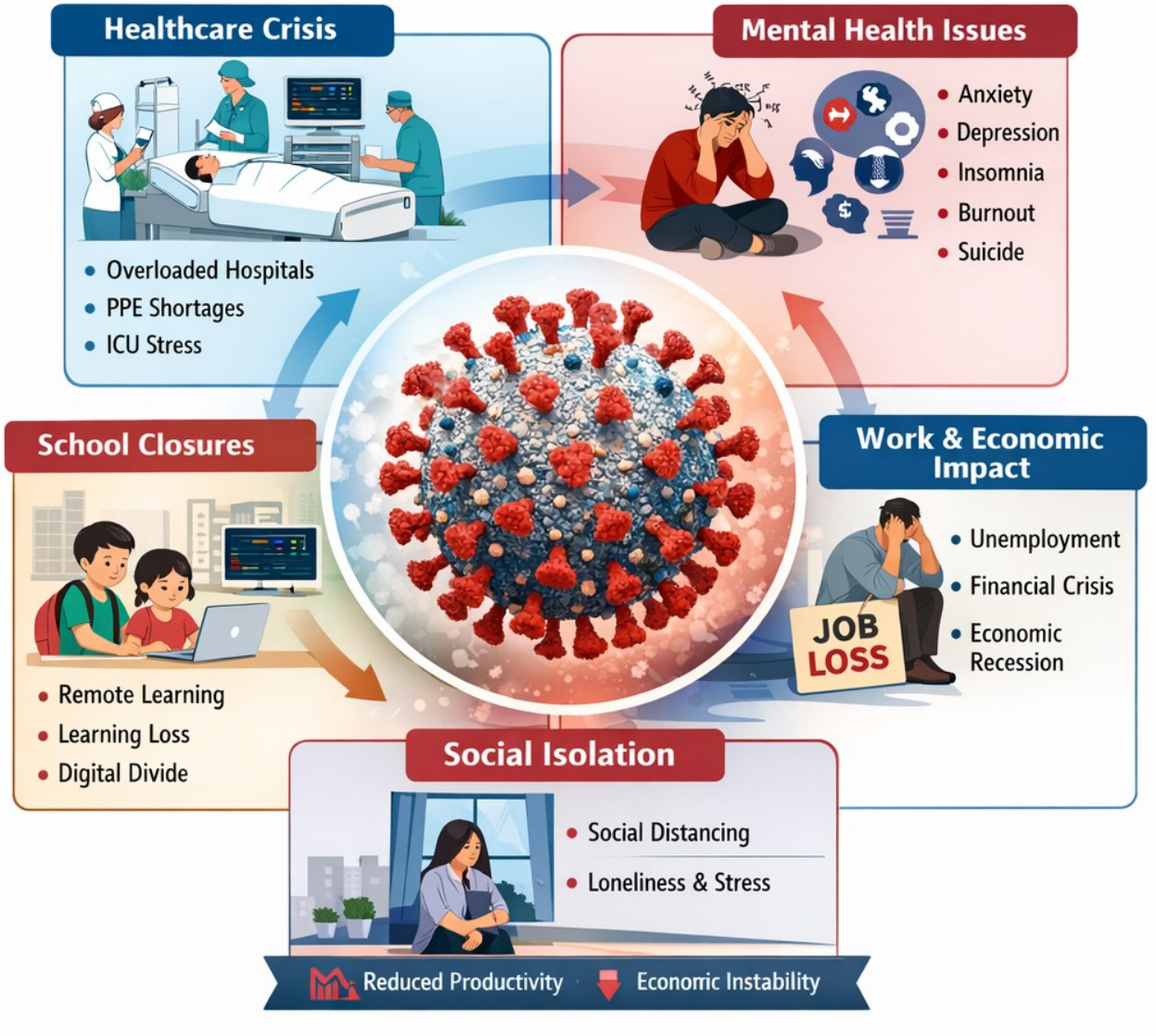

Fig. 1: Multidimensional impact of the COVID-19 pandemic.

Table 1: Key impacts of COVID-19 across major sectors

Sector	Major Impacts	Reported Outcomes

Healthcare	Shortage of PPE, ventilators, ICU beds	Increased workload, staff burnout, and delayed care
Mental Health	Anxiety, depression, insomnia, loneliness	Increased suicide rates, psychological distress
Education	School and university closures	Learning loss, digital divide, and delayed examinations
Workforce	Lockdowns and unemployment	Reduced productivity, financial insecurity
Public Health	Social distancing and isolation	Reduced transmission but increased loneliness

In Silico vaccine design for COVID-19

Bioinformatics integrates computational modeling, immunoinformatics, and systems biology to support rapid vaccine [84-89] and therapeutic development against cancer [90-94], neurological disorders [95-102] and emerging viral diseases like COVID-19. *In*

silico vaccine design has played a critical role in accelerating COVID-19 vaccine development by utilizing computational tools to identify immunogenic epitopes from SARS-CoV-2 proteins, particularly the spike glycoprotein. Immunoinformatics approaches enabled the prediction of B-cell and T-cell epitopes, population coverage analysis, molecular docking with immune receptors, and safety assessment of vaccine candidates. These methods significantly reduced time and cost compared to traditional vaccine development, guiding experimental validation and contributing to the rapid development of effective COVID-19 vaccines.

Conclusion

The COVID-19 pandemic has profoundly affected global health, education, and socioeconomic systems. Beyond its clinical manifestations, the pandemic placed immense pressure on healthcare infrastructures, exposed frontline workers to psychological stress, and significantly disrupted educational systems worldwide. Lockdowns and social isolation contributed to rising mental health challenges, including anxiety, depression, insomnia, burnout, and suicide risk. Educational inequalities widened due to limited access to digital resources, particularly in low- and middle-income regions. Despite these challenges, adaptive strategies such as telemedicine, online education, and public health interventions helped mitigate some effects. Lessons learned from COVID-19 emphasize the importance of preparedness, mental health support, and technological integration for future global health crises.

Conflict of interest

The authors declare no conflict of interest.

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